ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: March 31, 2014

ClinicalTrials.gov ID: NCT01712334

Study Identification

Unique Protocol ID:	ML28249
Brief Title:	A Study of the Comparable Efficacy and Safety of Pulmozyme (Dornase Alfa) Delivered by the eRapid Nebulizer System in Patients With Cystic Fibrosis
Official Title:	A Phase IV Multicenter, Randomized, Open Label, Two-Period, Crossover Study in Patients With Cystic Fibrosis to Evaluate the Comparable Efficacy and Safety of Pulmozyme Delivered by the eRapid Nebulizer System
Secondary IDs:	

Study Status

Record Verification:	March 2014
Overall Status:	Completed
Study Start:	December 2012 []
Primary Completion:	June 2013 [Actual]
Study Completion:	June 2013 [Actual]

Sponsor/Collaborators

Sponsor:	Genentech, Inc.
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	

U.S. FDA-regulated Device:	
Unapproved/Uncleared Device:	No
U.S. FDA IND/IDE:	Yes
IND/IDE Information:	FDA Center: CDER IND/IDE Number: 3537 Serial Number: 0343 Has Expanded Access No
Human Subjects Review:	Board Status: Approved
Data Monitoring:	
FDA Regulated Intervention:	Yes
Section 801 Clinical Trial:	Yes

Study Description

Brief Summary:	This phase IV, multicenter, randomized, open-label, two-period crossover study will evaluate the comparable efficacy and safety of Pulmozyme (dornase alfa) delivered by the eRapid nebulizer system in patients with cystic fibrosis. Patients who have been receiving Pulmozyme once daily chronically for at least 6 months will continue to receive Pulmozyme once daily for a run-in period of 2 weeks using the Pari LC Plus nebulizer. Patients will then be randomized to receive in a crossover design Pulmozyme once daily for two treatment periods of 2 weeks each using either the Pari LC Plus or the eRapid nebulizer. Anticipated time on study treatment is 6 weeks.
Detailed Description:	

Conditions

Conditions:	Cystic Fibrosis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Interventional Study Model:	Crossover Assignment
Number of Arms:	2

Masking:	None (Open Label)
Allocation:	Randomized
Enrollment:	99 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: eRapid Nebulizer Dornase alfa (Pulmozyme®) inhaled once daily by the Pari eRapid nebulizer for 2 weeks.	Drug: dornase alfa [Pulmozyme®] Inhaled once daily by Pari eRapid nebulizer.
Active Comparator: Jet Nebulizer Dornase alfa (Pulmozyme®) inhaled once daily by the Pari LC Plus jet nebulizer for 2 weeks.	Drug: dornase alfa [Pulmozyme®] Inhaled once daily by Pari LC Plus jet nebulizer.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	6 Years
Maximum Age:	
Sex:	All
Gender Based:	
Accepts Healthy Volunteers:	No
Criteria:	Inclusion Criteria:

- Male and female patients, >/= 6 years of age
- Confirmed diagnosis of cystic fibrosis (CF)
- Receiving Pulmozyme once daily chronically for treatment of CF for at least 6 months prior to screening
- Percent predicted FEV1 >/= 40% at screening based on the Wang (males < 18 years, females < 16 years) or Hankinson (males >/= 18 years, females >/= 16 years) standardized equations
- Able to reproducibly perform spirometry testing and comply with study assessments

Exclusion Criteria:

- An acute respiratory infection or pulmonary exacerbation within 4 weeks prior to randomization
- Initiation of any new chronic therapy (e.g. inhaled corticosteroids, inhaled oral antibiotics, high-dose ibuprofen, hypertonic saline, ivacaftor) for respiratory disease within 4 weeks prior to randomization
- Changes in chest physiotherapy schedule within 4 weeks prior to randomization

- Hospitalization within 4 weeks prior to randomization
- Planned hospitalization during the 6-week study
- History of organ transplantation
- Participation in an investigational drug or device study within 30 day prior to screening

Contacts/Locations

Central Contact Person: Reference Study ID Number: ML28249 www.roche.com/about_roche/roche_worldwide.htm
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Central Contact Backup:

Study Officials: Clinical Trials
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IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information:

Study Results

Participant Flow

Recruitment Details	99 patients were enrolled. 96 unique patients entered the run-in period including 3 patients who entered the run-in period twice.

Pre-assignment Details	Patients received dornase alfa (Pulmozyme®) by LC Plus nebulizer in the 2-week run-in period prior to randomization. A total of 86 unique patients were randomized in the study in 87 randomization events. Of the randomized patients, 85 patients completed the study in two treatment sequences.

Reporting Groups

	Description
eRapid Nebulizer Then Jet Nebulizer	Dornase alfa (Pulmozyme®) inhaled once daily by the Pari eRapid nebulizer for 2 weeks in Treatment Period 1 then Pulmozyme® inhaled once daily by the Pari LC Plus jet nebulizer for 2 weeks in Treatment Period 2. .
Jet Nebulizer Then eRapid Nebulizer	Pulmozyme® inhaled once daily by the Pari LC Plus jet nebulizer for 2 weeks in Treatment Period 1 then Pulmozyme® inhaled once daily by the Pari eRapid nebulizer for 2 weeks in Treatment Period 2.

Treatment Period 1

	eRapid Nebulizer Then Jet Nebulizer	Jet Nebulizer Then eRapid Nebulizer
Started	44	43
Received Treatment	44	41
Completed	44	41
Not Completed	0	2
Randomized in Error	0	2

Treatment Period 2

	eRapid Nebulizer Then Jet Nebulizer	Jet Nebulizer Then eRapid Nebulizer
Started	44	41
Completed	44	41
Not Completed	0	0

Baseline Characteristics

Baseline Analysis Population Description

Baseline measures were based on the modified Intent-to-Treat (mITT) population that included all participants randomized with both baseline and endpoint Forced Expiratory Volume in 1 second (FEV1) values for both treatment periods.

Reporting Groups

	Description
All Participants	All participants received dornase alfa (Pulmozyme) inhaled once daily by the Pari eRapid nebulizer or the Pari LC Plus jet nebulizer for 2 weeks in Treatment Period 1 then crossed over to use the other nebulizer in Treatment Period 2 for 2 weeks.

Baseline Measures

		All Participants
Overall Number of Participants		85
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	85 participants
		13.6 (6.92)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	85 participants
	Female	43 50.59%
	Male	42 49.41%

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Stability of Lung Function: Percent Predicted Forced Expiratory Volume in 1 Second (FEV1)
Measure Description	Spirometry was performed according to American Thoracic Society standards. FEV1 is the amount of air that is forced out of the lungs in one second and was measured at the end of each 2-week treatment period. The percent predicted FEV1 was calculated as: Percent predicted FEV1 =FEV1 (L) / Predicted FEV1 (L) ×100.
Time Frame	At the end of each 2-week treatment period

Analysis Population Description

Modified Intent-to-Treat (mITT) population included all randomized participants with baseline and endpoint FEV1 values for both treatment periods.

Reporting Groups

	Description
eRapid Nebulizer	Dornase alfa (Pulmozyme®) inhaled once daily by the Pari eRapid nebulizer for 2 weeks.
Jet Nebulizer	Pulmozyme® inhaled once daily by the Pari LC Plus jet nebulizer for 2 weeks.

Measured Values

	eRapid Nebulizer	Jet Nebulizer
Overall Number of Participants Analyzed	85	85
Stability of Lung Function: Percent Predicted Forced Expiratory Volume in 1 Second (FEV1) Mean (Standard Deviation) Unit of measure: percent predicted	98.1 (22.1)	97.2 (20.7)

Statistical Analysis 1 for Stability of Lung Function: Percent Predicted Forced Expiratory Volume in 1 Second (FEV1)

Statistical Analysis Overview	Comparison Group Selection	eRapid Nebulizer, Jet Nebulizer
	Comments	[Not specified]
	Type of Statistical Test	Non-Inferiority or Equivalence (legacy)
	Comments	The ratio of the mean percent predicted FEV1 at the end of the eRapid treatment to the mean percent predicted FEV1 at the end of the LC Plus jet nebulizer treatment. The two nebulizers were considered equivalent if the 90% CI was within 80%−125%.

Method of Estimation	Estimation Parameter	Other [Ratio (Fieller's theorem)]
	Estimated Value	100.9
	Confidence Interval	(2-Sided) 90% 99.5 to 102.3
	Estimation Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	Safety: Number of Participants With Adverse Events During Each Treatment Period
Measure Description	An adverse event was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study and laboratory or clinical tests that resulted in a change in treatment or discontinuation from study drug were reported as adverse events.
Time Frame	4 Weeks

Analysis Population Description

Safety population included all randomized participants who received treatment.

Reporting Groups

	Description
eRapid Nebulizer	Dornase alfa (Pulmozyme®) inhaled once daily by the Pari eRapid nebulizer for 2 weeks.
Jet Nebulizer	Pulmozyme® inhaled once daily by the Pari LC Plus jet nebulizer for 2 weeks.

Measured Values

	eRapid Nebulizer	Jet Nebulizer
Overall Number of Participants Analyzed	85	85
Safety: Number of Participants With Adverse Events During Each Treatment Period Measure Type: Number Unit of measure: participants	18	24

Reported Adverse Events

Time Frame	[Not specified]
Adverse Event Reporting Description	Safety population included all randomized participants who received treatment.

Reporting Groups

	Description
eRapid Nebulizer	Dornase alfa (Pulmozyme®) inhaled once daily by the Pari eRapid nebulizer for 2 weeks.
Jet Nebulizer	Pulmozyme® inhaled once daily by the Pari LC Plus jet nebulizer for 2 weeks.

All-Cause Mortality

	eRapid Nebulizer	Jet Nebulizer
	Affected/At Risk (%)	Affected/At Risk (%)
Total All-Cause Mortality	/	/

Serious Adverse Events

	eRapid Nebulizer	Jet Nebulizer
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/85 (0%)	0/85 (0%)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	eRapid Nebulizer	Jet Nebulizer
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/85 (0%)	0/85 (0%)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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